REMARKS

Claim 1 has been amended. Claims 2, 3, 5, and 7-12 were previously canceled and claim 13 was previously added. Accordingly, upon entry of the above amendments, claims 1, 4, 6, and 13 will be pending and under consideration in the above-identified application.

Claim Rejection Under 35 U.S.C. § 112

Claims 1, 4, 6, and 13 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the term "the water-soluble bivalent metal compound" in line three of claim 1 lacks proper antecedent basis.

The rejection has been overcome by the above amendment to claim 1 in which the limitation "the water-soluble bivalent metal compound" has been replaced with the limitation "a water-soluble bivalent metal compound."

Claim Rejections Under 35 U.S.C. § 102

Claim 1 stands rejected under 35 U.S.C. § 102(e) as being anticipated by Mizushima et al. (U.S. Patent Application Publication No. 2006/0093670).

Claim 1 requires that the drug-containing sustained release microparticle preparation includes a drug that is absorbed into "a zinc-containing porous hydroxyapatite which is formed by partially substituting calcium atoms of porous hydroxyapatite with zinc atoms."

Mizushima et al. 2006/0093670 does not anticipate the claimed invention because it does not disclose "a zinc-containing porous hydroxyapatite which is formed by partially substituting calcium atoms of porous hydroxyapatite with zinc."

It is apparent that the rejection is based on either a misunderstanding of what is being claimed or a misunderstanding of what Mizushima et al. 2006/0093670 is disclosing. The hydroxyapatite disclosed in the Mizushima et al. 2006/0093670 reference is an ordinary hydroxyapatite composition having the formula $Ca_5(PO_4)_3OH$. This is different from the hydroxyapatite of the claimed invention which has a formula $Ca_{(5-x)}Zn_x(PO_4)_3OH$.

Fundamental to the invention, the claims require a hydroxyapatite in which some of the calcium in the hydroxyapatite structure is replaced with zinc. Replacing calcium atoms in the structure of the hydroxyapatite with zinc atoms is not the same as contacting the hydroxyapatite

with a zinc salt. Merely contacting a hydroxyapatite of formula $Ca_5(PO_4)_3OH$ does not result in substitution of calcium atoms in the hydroxyapatite with zinc atoms.

Applicants appreciate the Examiner's argument that "claim 1 does not require any specific quantity of zinc substitution for calcium in the hydroxyapatite structure," and therefore, "a porous hydroxyapatite having a single atom of calcium displaced by zinc and having an absorbed drug reads on Applicants' claim 1." Nevertheless, Mizushima et al. 2006/0093670 does not disclose a hydroxyapatite in which even a single atom of calcium is displaced by zinc. The zinc acetate added to the drug-loaded hydroxyapatite particles of Example 2 of Mizushima et al. are not incorporated into the structure of the hydroxyapatite, but rather are physically absorbed into pores of the hydroxyapatite. Such absorption does not result in substitution of calcium atoms in the structure of the hydroxyapatite with zinc atoms.

It is respectfully submitted that the person having ordinary skill in the art would not have any difficulty understanding the very substantial and fundamental differences between the claimed invention and the compositions described by Mizushima et al. 2006/0093670. In view of the very substantial, fundamental, and easily understood differences between the claimed invention and the compositions disclosed by Mizushima et al. 2006/0093670, a withdrawal of the rejection is appropriate and necessary to avoid reversible error.

Rejections Under 35 U.S.C. § 103

Claims 4, 6, and 13 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Mizushima et al. 2006/0093670 in view of Tomlinson et al. (U.S. Patent No. 4,157,378).

The rejection of dependent claims 4, 6, and 13 is improper for the reasons set forth above with respect to independent claim 1. Specifically, Mizushima et al. 2006/0093670 and/or the combination of Mizushima et al. in view of Tomlinson et al. '378 do not teach, suggest, motivate, or provide any reason for preparing a dosage form by absorbing a drug in "a zinc-containing porous hydroxyapatite which is formed by partially substituting calcium atoms of porous hydroxyapatite with zinc."

As stated above, Mizushima et al. 2006/0093670 employs ordinary hydroxyapatite having formula $Ca_5(PO_4)_3OH$ in which not even a single atom of calcium has been replaced with zinc.

The Tomlinson et al. '378 reference does not overcome this deficiency. While Tomlinson et al. '378 discloses that zinc-substituted apatites can be prepared by placing a hydroxyapatite in a container with an aqueous solution of zinc nitrate in which the pH is caused to fluctuate between about 7 and 4 several times, such pH fluctuations are not inherent or suggested by Mizushima et al., and Tomlinson et al. does not recognize the benefits of employing such zinc-substituted hydroxyapatites in a drug-containing sustained release preparation in which both a drug other than human growth hormone and a water-soluble bivalent mineral compound are absorbed.

Moreover, the prior art combination does not lead the person having ordinary skill in the art to expect a beneficial result will be achieved by absorbing a drug and a divalent cation into zinc-substituted hydroxyapatite particles. In fact, it is impossible for the person having ordinary skill in the art to foresee or know, as shown in Table 1 of the specification, that the zinc-substituted hydroxyapatite of the invention has better effect in absorption of a drug than the ordinary, unsubstituted hydroxyapatite having formula $Ca_5(PO_4)_3OH$. As can be seen by reference to Table 1, a much larger amount of steroid can be absorbed into a porous hydroxyapatite in which calcium atoms in the hydroxyapatite structure have been substituted with zinc atoms.

In view of the unexpected benefits and the absence of any reason in the prior art to absorb a drug and a bivalent metal compound in a zinc-modified porous hydroxyapatite, it is respectfully submitted that the rejection is inappropriate and should be withdrawn.

Double Patenting Rejection

Claims 1, 4, 6, and 13 have been provisionally rejected on ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 7, 23, and 25 of co-pending Application No. 10/516,122.

As stated above, the Mizushima et al. 2006/0093670 reference (corresponding with Application No. 10/516,122) does not teach, suggest, or provide any motivation or reason for employing the required "zinc-containing porous hydroxyapatite which is formed by partially substituting calcium atoms of porous hydroxyapatite with zinc." Hydroxyapatite does not inherently have zinc atoms substituted for calcium atoms, and such substitution cannot be achieved by merely combining a bivalent metal salt with unmodified hydroxyapatite particles. Rather, as

taught by the cited and applied Tomlinson et al. '378 reference, relatively harsh conditions must deliberately be applied in order to achieve the desired substitution. Such conditions are not disclosed by Mizushima et al. 2006/0093670, such that zinc substitution cannot occur, even inadvertently at very low levels.

In view of the fundamental differences between the claimed invention and the compositions disclosed and claimed by Mizushima et al., it is submitted that the rejection is inappropriate, and that a failure to withdraw the rejection would constitute reversible error.

CONCLUSION

In view of the above amendments and remarks, it is evident that the claims are in condition for allowance and notice of the same is requested.

Respectfully submitted,

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